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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,737	10/15/2003	Richard A. Rubin	97,022-D1-CO	6145
20306	7590	05/04/2006		EXAMINER
				SKIBINSKY, ANNA
			ART UNIT	PAPER NUMBER
				1631

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/685,737	RUBIN ET AL.
Examiner	Art Unit	
Anna Skibinsky	1631	

**– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –**

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 13 March 2006.

2a)  This action is FINAL.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 40-43 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5)  Claim(s) \_\_\_\_\_ is/are allowed.  
6)  Claim(s) 40-43 is/are rejected.  
7)  Claim(s) \_\_\_\_\_ is/are objected to.  
8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All    b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 6 pages.

4)  Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_

5)  Notice of Informal Patent Application (PTO-152)

6)  Other: \_\_\_\_\_

## DETAILED ACTION

### *Reply to Applicant*

Applicant's election with traverse of Species A1 and B1 in the reply filed on March 13, 2006 is acknowledged. The traversal is on the ground(s) that the computerized method claimed would be equally carried out on living cells as well as non-living cells. This is found persuasive and the species are rejoined.

### ***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 40 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Marks et al.

1. Claim 40 recites identifying internalizing cell surface receptor proteins in cells where individual cells comprise a first luminescent reporter molecule that reports on the cell surface receptor and a second luminescent reporter molecule that identifies cells. Identifying internalized cell surface receptors by determining a luminescent signal from the first reporter molecule that surpasses a user defined intensity.

2. Marks et al. teach a method of internalizing phages into target cells and identifying the internalized phages (Abstract). This includes identifying internalizing antibodies as well as internalizing receptors (col. 1, lines 20-25). The method can be

carried out by labeling the phage with a reporter gene encoding a fluorescent protein such as GFP or a luciferase (col. 2, line 66 to col. 3, line 5; and col. 4, lines 9-12).

3. Marks et al. teaches a method of identifying internalizing receptors (col. 13, lines 44-55) as well as using reporter genes to identify cells that express GFP. This method can be used to identify target cells (col. 17, line 45 to col. 18, line 22) within a subtractive cell line (col. 18, lines 23-65). Here, the subtractive cells display all the markers of the target cell except the marker (e.g. receptor) that is to act as a target for the desired binding of antibodies or binding polypeptides. This reads on the limitations set forth in claim 40(a) where each cell is contacted with at least two reporter molecules.

4. Marks et al. goes on to teach identification of an internalized phage (col. 19, line 57 to col. 20, line 10) with the use of a detectable fluorescent signal where the phage bears a marker (e.g. label) and the surface bound or internalized phages are sorted (col. 20, lines 3-14).

5. The prior art of Marks et al. teaches the measuring of internalized phages with FAC (fluorescence activated cell sorting) and expressed in MFI or percent of positively fluorescing cells (col 46, lines 47-48 ;col. 47, line 65 to col. 48, line 3; and Figure 9). This reads on the limitations set forth in claim 40(b) where calculations provide a measurement of the internalization of the cell surface receptor in individual cells.

6. Claim 41 recites the steps (a) and (b) carried out at multiple time points. As illustrated in Figure 9, the internalization of the phages are calculated at multiple time points.

***Claim Rejections - 35 USC § 112***

***New Matter***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 40-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. Claim 40 recites a cell with two luminescent reporter molecules, one which identifies the cell and another which reports on an internalizing cell surface receptor. Applicant has pointed specifically to Example 4, pages 64 to 67 which describe the staining of the nucleus and the calculation of "spot areas" taken from cell images. However, the example does not illustrate the reporting of internalizing cell surface receptors. This appears in the original claims as filed but the original claims do not however contain the second reporter molecule which identifies the cells.

10. Claims 42 to 43 recite calculating normalized aggregate intensities, the area, the number of objects that represent internalized cell surface receptors, and obtaining high and low resolutions, however, support for these limitations were not pointed to in the specifications or the claims as originally filed and none were found.

11. This is deemed **NEW MATTER**.

*Vague and Indefinite*

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 40(a), line 5 recites "internalized cell surface receptor proteins" which is vague as to whether the "internalized" defines the state of the cell surface protein or the name. For example, transferrin is an internalized surface receptor which exists on the surface of the cell before being internalized. Does the claim intend to recite a cell surface receptor that can be internalized or one that has already been internalized? Clarification of "internalized cell surface receptor" as used in the claim is requested.

15. Claim 40(a), lines 7-10 recite a first reporter molecule that reports on a cell surface receptor and a second reporter molecule that identifies cells wherein the identifying comprises determining the luminescent signals from the first luminescent reporter molecule on or in cells identified by the second reporter molecule. It is unclear if this second reporter molecule identifies the cells that have the internalized surface cell receptor or just the cells being studied, whether they contain they internalized receptor or not. The claim recites a first reporter molecule that "reports" and a second reporter molecule that "identifies" and then goes on to recite that identifying comprises the

determining of the luminescent signals from the first reporter molecule. Clarification is  
quested.

***Claim Rejections - 35 USC § 101***

16. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 40-43 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Said claims are toward a computer implemented method involving a program within a machine readable storage medium. Though the properties calculated by the model are physical properties pertaining the identification of internalized cell surface receptors, the data is none-the-less generated within a computer without a physical manifestation or transformation such as movement from a storage device (i.e. memory) to a processor or the displaying of data on a computer screen. Thus, these claims do not produce a result which meet the standard of being concrete, tangible and useful.

The claims "must be for a practical application of the abstract idea, law of nature, or natural phenomenon. Diehr, 450 U.S. at 187, 209 USPQ at 8 ("application of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection."); Benson, 409 U.S. at 71, 175 USPQ at 676 (rejecting formula claim because it "has no substantial practical application").

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways:

1) The claimed invention "transforms" an article or physical object to a different state or thing.

2) The claimed invention otherwise produces a useful, concrete and tangible result, based on the factors discussed in MPEP 2106, and See also:

[http://www.uspto.gov/web/offices/pac/dapp/opla/preognote/guidelines101\\_20051026.pdf](http://www.uspto.gov/web/offices/pac/dapp/opla/preognote/guidelines101_20051026.pdf)

The manipulation of coordinates and interaction energies or residues to calculate the crossover point is the manipulation of numbers, performed by the computer implementing programs and is therefore nonstatutory subject matter. Manipulation of data does not include a physical transformation outside of a computer or representation thereof. A process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and is not deemed to be concrete, tangible, and useful and is therefore non-statutory. An example which would make the instant method steps statutory would be to include a step of displaying the data for a user. Hence, the data would become concrete, tangible, and useful.

### Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anna Skibinsky whose telephone number is (571) 272-4373. The examiner can normally be reached on 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Anna Skibinsky, Ph.D.

  
JOHN S. BRUSCA, PH.D.  
PRIMARY EXAMINER